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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/781,841	02/20/2004	Masato Horie	Q-76526	5773

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EXAMINER	
WHITEMAN, BRIAN A	
ART UNIT	PAPER NUMBER
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/781,841	HORIE, MASATO	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/7/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 30-33 are pending.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 11/7/06 is being considered by the examiner. The IDS was submitted before the first office action and applicant was supplying the authors of the articles listed on the IDS, but not considered because they were missing the author's name.

Claim Rejections - 35 USC § 101 and 35 USC § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30-33 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by a substantial or well-established utility.

The instant specification contemplates that the novel human NRP1 gene is provided and the use of said gene makes it possible to detect the expression of said gene in various tissue and product the human NRP1 protein by the technology of genetic engineering. NRP1 can further be to study in brain neurotransmission system, diagnosis of various diseases related to

neurotransmission in the brain, and the screening and evaluation of drugs for the treatment and prevention of such diseases (page 90-91). The NRP might be secretory proteins or proteins anchored to membranes as a result of posttranslationation modification (page 89). The applicant speculates that NRP might function as ligands by stimulating other molecules such as EGF receptors (page 89). Furthermore, the EGF-domain containing NRP could act as growth factors in brain and may be useful in the diagnosis and treatment of various kinds of intracerebral tumor and effective in nerve regeneration in cases of degenerative nervous diseases (page 91). The domains of NRP suggest that NRPs might play a role as signal molecules for growth regulation (page 90). Applicant further suggests that these genes might have particular function in kidney (page 90).

The claims are drawn to an isolated nucleic acid molecule encoding a nel-related protein type 1 (NRP1, also known as NELL1) consisting of the DNA sequence in SEQ ID NO: 35. At the time the invention was made, it was unknown that SEQ ID NO: 35 or a nucleic acid sequence encoding SEQ ID NO: 34 were associated with a role in having cranial nerve growth activity and/or nerve regenerating activity. The instant specification does not teach what activity is related with expression of NRP1. The instant specification provides no nexus between the 'association' of the claimed nucleic acid molecule with cranial nerve growth and/or nerve regeneration.

With respect to using the claimed polynucleotides or products made directly or indirectly from the nucleic acid molecule in either an *in vitro* or an *in vivo* screening assay comprising observing an increase or a decrease of the claimed DNA products or NRP1-associated gene products, the instant specification does not teach what to look for as a result of an increase or a

decrease in expression of SEQ ID NO: 34 encoded by a DNA sequence or a polynucleotide comprising SEQ ID NO: 35. One skilled in the art would have to further experiment on the invention to determine what results are observed with either an increase or a decrease in expression of SEQ ID NO: 34 in a genus of cells, including neurons (nerve cells). In absence of the instant specification teaching what to look for in the assays, the claimed invention lacks utility.

In addition, with respect to using the claimed nucleic acid molecule or products made directly or indirectly from the sequences, the instant specification provides no evidence that SEQ ID NO: 35 or a nucleic acid encoding SEQ ID NO: 34 is involved in intracerabral tumor or degenerative nerve diseases. The specification provides no evidence that the claimed DNA sequences are associated with any specific disease (e.g., tumor, kidney disease, degenerative nervous disease). It would require further experimentation on the claimed invention/or products made directly or indirectly from the DNA sequences to determine whether they were involved in intracerabral tumor or other disease(s). Thus, the asserted utilities set forth above do not provide a benefit to the public in currently available form. See Ziegler, 992 F.2d at 1203, 26 USPQ2d 1600 (Fed. Cir. 1993).

At pages 88-89 of the specification, the applicant teaches the result of homology analysis for NRPs and nel. The applicant and prior art teach that NRP1 has 50% homology to chick embryonic nel (page 88). NRP1 is considered not to be a human counterpart of nel, but a homologous gene (page 89). The domains of NRP suggest that NRPs might play a role as signal molecules for growth regulation (page 90). The instant specification and the prior art are absent for an undefined NRP protein having several EGF-like repeats. The skilled artisan understands

that EGF repeats are present in several proteins with different functions. At page 90, applicant teaches that Northern blot analysis, it was found that NRP1 was weakly expressed in fetal and adult brain and kidney. The office conducted a sequence search of the polynucleotide sequence set forth in SEQ ID NO: 35 against nucleotide public databases. The results from the polynucleotide sequence databases search did not display any sequence similarity with any known gene associated with cranial nerve growth and/or nerve regenerating activity. Sequences, at the time the application was filed, with the closest sequence similarity with SED ID NO: 35, besides nel, is fibrillin I, 11.7% identity (calcium-binding protein). Furthermore, a post-filing reference teaches that the precise role of Nell-1 is unknown (see Ting et al. Journal of Bone and Mineral Research, 14:80-89, 1999).

Since the claimed invention is not supported by either a substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention. See also In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967) and In Brenner v. Manson, 383 US 519, 148 USPQ 689 (1966). Also see REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS: www.uspto.gov/web/menu/utility.pdf.

Applicant's arguments filed 11/7/06 have been fully considered but they are not persuasive for the following reason(s):

The Declaration under 37 CFR 1.132 filed 11/7/06 is insufficient to overcome the rejection of claims 30-33 based upon 101 rejection as set forth in the last Office action because: the product (rat NPR1) tested by applicant is not the product recited in the instant claims. The applicant states that rat NPR1 DNA has about 93% homology to human Nell1 DNA. The applicant does not indicate if the Nell1 DNA in Kang is the DNA recited in the instant claims.

The skilled artisan understands that even one nucleotide change in a polynucleotide sequence or one amino acid change in a polypeptide sequence can change the function of the protein. See Lucentini, The Scientist, 18:20, 2004. Thus, the skilled artisan would not be able to reasonably extrapolate from the teaching in the specification to the activity of the rat NRP1 protein.

Claims 30-33 remain also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a well asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicant's arguments filed 11/7/06 have been fully considered but they are not persuasive for the reasons set forth under the 101 rejection.

Response to Arguments

Applicant's arguments, see page 4, filed 11/7/06, with respect to 102(a) have been fully considered and are persuasive. The rejection of claim 30 has been withdrawn because the applicant has filed a certified translation of the foreign priority documents.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Douglas Schultz, PhD, SPE – Art Unit 1635, can be reached at (571) 272-0763.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system

provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Brian Whiteman